PATENTS
Attorney Docket No. 25352-0022

CERTIFICATE OF FACSIMILE TRANSMISSION

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Sam L. Nguyen, Reg. No. 52,496 — March 11, 2004 Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hugo O. Villar et al. : Confirmation No.: 2049

App. No.: 10/082,801 : Art Unit: 1614

Filed: 22 February 2002 : Examiner: Brian Yong S. Kwon

For: Acridines as stimulators for Fas-mediated apoptosis

Commissioner for Patents
PO Box 1450
Alexandria VA 22313-1450

Sir:

TRANSMITTAL

Transmitted herewith is a response to the Office Action mailed 11 September 2003, totaling, together with this Transmittal, 6 pages.

Please charge the fee for a three-month extension of the period for response ($950), and any other fees that may be necessary, to our deposit account 08-1641, referring to 25352-0022.

Respectfully submitted,

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11 March 2004

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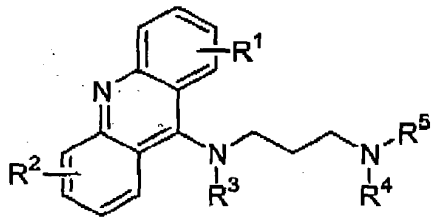
RESPONSE TO OFFICE ACTION

In response to the Office Action mailed 11 September 2003, for which a three-month extension of the period for response is requested in the accompanying Transmittal, so that the due date for the response is 11 March 2004, please enter the following amendment and consider the following remarks.

Claim amendments

1. (Currently amended) A method of treating an autoimmune, infectious, or hyperplasic disease selected from autoimmune lymphoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma in a mammal, comprising administering to the mammal a therapeutically effective amount of a compound of the formula:



where:

R^1 and R^2 are ~~independently selected from~~ hydrogen~~, halogen, hydroxy, optionally substituted alkyl, optionally substituted alkyloxy, -NRR' (where R is hydrogen or alkyl and R' is hydrogen, alkyl, or aryl), and optionally substituted aryl~~; and

R_3, R_4, and R_5 are independently selected from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted alkylcarbonyl, and optionally substituted arylcarbonyl,

as a single stereoisomer or mixture of stereoisomers,

or a pharmaceutically acceptable salt thereof.

2. (Canceled)

3. (Currently amended) The method of claim 1 2, where R^3 is hydrogen.

4. (Original) The method of claim 3, where R^4 and R^5 are alkyl.

5. (Original) The method of claim 4, where the compound is 9-[(3-diethylaminopropyl)amino]acridine or a pharmaceutically acceptable salt thereof.

6. – 8. (Canceled)

9. (Currently amended) The method of claim 1, further comprising treating said mammal with an additional form of therapy for said disease ~~state~~ , the additional form of therapy being a conventional form of therapy for said disease.

10. – 11. (Canceled)

12. (new) The method of claim 1, where the disease is a hyperplasic disease selected from colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma.

Remarks

The amendment

Entry of the amendment is respectfully requested.

No new matter is added by the amended/added claims, because each of the claims is supported by the application as filed. Amended claim 1 corresponds to original claim 2 limited to the set of diseases identified at page 1, line 24 – page 2, line 2 as being associated with Fas-mediated apoptosis; amended claim 3 has its dependency changed to reflect the addition of the subject matter of original claim 2 to amended claim 1; and amended claim 9 reflects the additional therapy being conventional for the disease (page 12, line 23). Redundant claims 2 and 6-8 have been canceled; and non-elected claims 10 and 11, withdrawn from consideration, have also been canceled. New claim 12 claims only hyperplasic diseases within the scope of claim 1.

The restriction requirement

Restriction had previously been required between claims 1-9 and 10-11, and Applicants had elected claims 1-9. The non-elected claims have now been canceled.

The 35 USC 112, ¶1 rejection

Original claims 1 and 7 were rejected under 35 USC 112, ¶1 for lack of enablement with respect to the full scope of autoimmune or hyperplastic diseases, while suggesting that the claims were enabled for those diseases reported to be associated with Fas-mediated apoptosis (autoimmune lymophoproliferative syndrome, autoimmune thyroid disease, hypereosinophilia, viral hepatitis, colon carcinoma, breast carcinoma, prostate cancer, neuroblastoma, and glioma). The Examiner's helpful suggestion has been followed and claim 1, the independent claim, has been amended to limit the diseases to that list. Withdrawal of the rejection is requested.

The 35 USC 112, ¶2 rejection

Original claim 9 was rejected under 35 USC 112, ¶2 for indefiniteness with respect to the "additional form of therapy", while suggesting clarification to a known conventional form of therapy. The Examiner's helpful suggestion has been followed and claim 9 has been amended to specify that the additional therapy be a conventional therapy for the disease (the word "known" has not been included because Appplicants believe it is implicit in "conventional"). Withdrawal of the rejection is requested.

The 35 USC 102(b) rejection

Original claims 1-4 and 7 were rejected under 35 USC 102(b) for anticipation by Radzikowski et al., *Archivum Immunologiae et Therapiae Experimentalis*, 1969, 17(1), 86-88 ("Radzikowski"). This rejection, as applied to the amended claims, is respectfully traversed.

The rejection asserts that Radzikowski "teaches the use of the claimed acridine derivatives represented by the formula (e.g. 9-(dimethylaminopropylamino)-4-methoxyacridine and 9-(dimethylaminopropylamino)-2-methylacridine)" for the treatment of hyperplasic disease. Claim 1 has been amended to limit the compounds claimed to only those where the benzene rings of the acridine are unsubstituted, and it is submitted that none of Radzikowski's compounds are unsubstituted. Withdrawal of the rejection is therefore requested.

The 35 USC 103(a) rejections

Original claims 5 and 9 were rejected under 35 USC 103(a) for obviousness over Radzikowski. This rejection, as applied to the amended claims, is respectfully traversed.

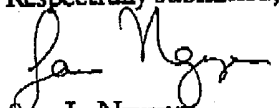
The rejection asserts that the teachings of Radzikowski differ from the claims in the use of 9-[(3-diethylaminopropyl)amino]acridine (claim 5) and combination with other known therapy (claim 9); and that each of these changes would be within the ordinary skill of the art. Applicants disagree. As discussed above with respect to the 35 USC 102(b) rejection, Radzikowski discloses no compounds that are unsubstituted on the benzene rings of the acridine – all are substituted with either methyl or methoxy. Further, as the rejection acknowledges, the closest 9-substitution of Radzikowski is the dimethylaminopropylamino group and not the diethylaminopropylamino group. Applicants submit that Radzikowski fails to suggest that compounds lacking substitution on the benzene rings of the acridine and/or having a diethylaminopropylamino substituent on the 9-position would have efficacy, and the rejection should be withdrawn as to claim 5 for that reason. With respect to claim 9, because Radzikowski discloses no compounds that are unsubstituted on the benzene rings of the acridine and fails to suggest that such compounds would be efficacious alone, there can be no suggestion that they would be efficacious in combination with an other known therapy. Withdrawal of the rejection is therefore requested.

Claim 6 was rejected under 35 USC 103(a) for obviousness over Petri et al., *Acta Microbiologica Hungarica*, 1995, 42(2), 203-208 ("Petri") in view of Armistead et al, US Patent No. 5,192,773 ("Armistead"). Claim 6 has been cancelled.

Conclusion

Entry of the amendment, and examination and allowance of the claims, are respectfully requested.

Respectfully submitted,



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